PURIFICATION OF CELL CULTURE-DERIVED INFLUENZA VIRUS VIA CONTINUOUS CHROMATOGRAPHY

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In vaccine production downstream processing often constitutes a bottleneck in terms of process productivity and economy. One way to design more efficient purification trains could be the implementation of continuous chromatographic methods.

The aim of this study was the purification of cell culture-derived influenza virus using continuous chromatography. Therefore, two chromatographic modes, flow through with CaptoCore (CC) beads and bind and elute with anion exchange (AEX) monoliths, were characterized for their ability to separate the virus from contaminating host cell protein and DNA. The starting material for the CC was treated with nuclease to decrease the DNA content and fragment size. Further, regeneration conditions for the chromatographic media, a prerequisite for successful continuous implementation, were identified and verified in sequential batch experiments.

Simulated moving bed chromatography (SMB) was performed in an open loop configuration using constant switching times. In case of the CC material, two columns were located in the separation zones and two additional columns were regenerated and equilibrated in detached zones. For the AEX runs, on the other hand, monoliths were used in a three zone configuration with detached high salt zone for regeneration.
Results in batch chromatography (BC) and SMB showed similar product yields in the range 60 to 100%. Contaminant depletion was >98% DNA and >58% protein for the AEX monoliths. Both the CC SMB and the BC resulted in comparable impurity levels (33.2 µg protein and 25.6 ng DNA per estimated 15 µg HA) but for BC a higher product yield (89% vs 72%) was achieved. In addition, the virus dilution during the flow through chromatography could be reduced in the cyclic steady state of the SMB by a factor of 1.8.

Overall, the separation performance of the BC has been successfully transferred to the continuous process.